TDMS No. 93020 - 07
Test Type: CHRONIC
Route: SKIN APPLICATION
Species/Strain: RATS/F 344

## P03: INCIDENCE RATES OF NON-NEOPLASTIC LESIONS BY ANATOMIC SITE(a)

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Final #2/Rats

C Number: C93020D

**Lock Date:** 03/14/2003

Cage Range: ALL

Date Range: ALL

**Reasons For Removal:** ALL

Removal Date Range: ALL

Treatment Groups: Include ALL

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Diamanitian Communication					
Disposition Summary					
Animals Initially in Study Early Deaths	50	50	50	50	
Moribund Sacrifice Natural Death	18 12	12 8	10 8	23 10	
Survivors					
Terminal Sacrifice Animals Examined Microscopically	20 50	30 50	32 50	17 50	
ALIMENTARY SYSTEM					
Intestine Large, Cecum	(50)	(50)	(50)	(49)	
Ulcer Edema	1 (2%) 1 (2%)	2 (4%)	4 (8%)	2 (4%)	
Hemorrhage Intestine Large, Colon	(50)	(50)	1 (2%) (50)	(50)	
Inflammation, Chronic Active	(00)	1 (2%)	(55)	(55)	
Intestine Small, Duodenum	(49)	(49)	(49)	(49)	
Epithelium, Hyperplasia		1 (2%)	2 (4%)	1 (2%)	
Liver	(50)	(50)	(50)	(50)	
Angiectasis	2 (4%)	2 (4%)	1 (2%)	1 (2%)	
Clear Cell Focus	16 (32%)	11 (22%)	14 (28%)	8 (16%)	
Mixed Cell Focus	4 (8%)	6 (12%)	6 (12%)	4 (8%)	
Basophilic Focus	14 (28%)	14 (28%)	22 (44%)	9 (18%)	
Hepatodiaphragmatic Nodule	5 (10%)	5 (10%)	7 (14%)	8 (16%)	
Eosinophilic Focus	6 (12%)	2 (4%)	7 (14%)	4 (8%)	
Degeneration, Cystic	3 (6%)	5 (10%)	4 (8%)		
Necrosis, Focal		1 (2%)	1 (2%)		
Infiltration Cellular, Mixed Cell		2 (4%)	4 (8%)		
Regeneration		1 (2%)	1 (2%)	4 (00()	
Hemorrhage			2 (4%)	1 (2%)	
Metaplasia, Atypical				1 (2%)	
Cyst	00 (000()	20 /700/\	04 (000()	1 (2%)	
Bile Duct, Hyperplasia	33 (66%)	36 (72%)	31 (62%)	17 (34%)	
Centrilobular, Necrosis	4 (8%)	3 (6%)	2 (4%)	4 (20/)	
Hepatocyte, Vacuolization Cytoplasmic	6 (12%)	6 (12%)	7 (14%)	1 (2%)	
Kupffer Cell, Pigmentation	(0)	2 (4%)	(12)	(6)	
Mesentery	(9)	(9)	(12)	(6)	

a - Number of animals examined microscopically at site and number of animals with lesion

**TDMS No.** 93020 - 07

Test Type: CHRONIC

Route: SKIN APPLICATION

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Accessory Spleen	1 (11%)				
Fat, Necrosis	7 (78%)	6 (67%)	8 (67%)	3 (50%)	
Pancreas	(50)	(50)	(50)	(50)	
Atrophy	18 (36%)	28 (56%)	32 (64%)	21 (42%)	
Cyst	2 (4%)	3 (6%)	5 (10%)	3 (6%)	
Hemorrhage	, ,	, ,	1 (2%)	,	
Acinus, Cytoplasmic Alteration		1 (2%)	1 (2%)	1 (2%)	
Acinus, Hyperplasia, Focal	2 (4%)	5 (10%)	4 (8%)	,	
Salivary Glands	(49)	(50)	(50)	(50)	
Atrophy	1 (2%)	,	1 (2%)	2 (4%)	
Necrosis	(		1 (2%)	1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(49)	
Inflammation, Chronic	2 (4%)	1 (2%)	()	2 (4%)	
Ulcer	7 (14%)	6 (12%)	6 (12%)	2 (4%)	
Erosion	1 (2%)	1 (2%)	1 (2%)	= ( · / • /	
Edema	3 (6%)	3 (6%)	5 (10%)	2 (4%)	
Perforation	1 (2%)	- (-,-)	1 (2%)	= ( · / • /	
Diverticulum	. (= /3)	1 (2%)	. (= /3)		
Epithelium, Hyperplasia	7 (14%)	6 (12%)	8 (16%)	5 (10%)	
Stomach, Glandular	(50)	(50)	(50)	(49)	
Inflammation, Chronic	1 (2%)	1 (2%)	(33)	(10)	
Erosion	7 (14%)	6 (12%)	3 (6%)	3 (6%)	
Ulcer	4 (8%)	2 (4%)	3 (6%)	1 (2%)	
Cyst	. (6,5)	1 (2%)	1 (2%)	. (= /=)	
Edema		2 (4%)	. (= /3)		
Glands, Hyperplasia	2 (4%)	_ ( . , 0 )	1 (2%)	1 (2%)	
	2 (170)		. (270)	. (=70)	
CARDIOVASCULAR SYSTEM					
Heart	(50)	(50)	(50)	(50)	
Cardiomyopathy	41 (82%)	44 (88%)	44 (88%)	36 (72%)	
Thrombosis	5 (10%)	1 (2%)	5 (10%)	33 (1270)	
Inflammation, Chronic	3 (1373)	1 (2%)	1 (2%)		
		1 (270)	1 (270)		
ENDOCRINE SYSTEM					
Adrenal Cortex	(50)	(49)	(50)	(50)	
Degeneration, Fatty	12 (24%)	11 (22%)	15 (30%)	8 (16%)	
Hyperplasia, Diffuse	1 (2%)	11 (22/0)	13 (3070)	3 (1370)	
Hyperplasia, Focal	8 (16%)	8 (16%)	5 (10%)	5 (10%)	
. Typotpiaola, i ooal	0 (1070)	3 (1070)	3 (1070)	3 (1370)	

a - Number of animals examined microscopically at site and number of animals with lesion

**TDMS No.** 93020 - 07

Test Type: CHRONIC

Route: SKIN APPLICATION

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Accessory Adrenal Cortical Nodule	17 (34%)	16 (33%)	16 (32%)	9 (18%)	
Hypertrophy, Focal	3 (6%)	2 (4%)	7 (14%)	3 (6%)	
Adrenal Medulla	(50)	(48)	(50)	(50)	
Hyperplasia	7 (14%)	9 (19%)	16 (32%)	3 (6%)	
Islets, Pancreatic	(50)	(50)	( <del>5</del> 0)	(50)	
Hyperplasia	2 (4%)	,	,	,	
Parathyroid Gland	(49)	(48)	(49)	(48)	
Hyperplasia	,	1 (2%)	,	,	
Hyperplasia, Focal		,		1 (2%)	
Pituitary Gland	(50)	(50)	(50)	(50)	
Pars Distalis, Angiectasis	,	4 (8%)	1 (2%)	2 (4%)	
Pars Distalis, Cyst	2 (4%)	3 (6%)	1 (2%)	1 (2%)	
Pars Distalis, Hyperplasia, Focal	3 (6%)	7 (14%)	7 (Ì4%)	5 (10%)	
Pars Intermedia, Cyst	,	1 (2%)	1 (2%)	1 (2%)	
Thyroid Gland	(50)	(50)	(50)	(50)	
Últimobranchial Cyst	1 (2%)	,	,	2 (4%)	
C-cell, Hyperplasia	8 (Ì6%́)	12 (24%)	3 (6%)	3 (6%)	
Follicle, Cyst	4 (8%)	5 (10%)	2 (4%)	3 (6%)	
Follicular Cell, Hyperplasia	3 (6%)	,	1 (2%)	,	
ENERAL BODY SYSTEM					
None					
ENITAL SYSTEM					
Epididymis	(50)	(50)	(50)	(50)	
Granuloma Sperm	()	(/	(/	1 (2%)	
Preputial Gland	(50)	(50)	(50)	(50)	
Inflammation, Chronic	18 (36%)	26 (52%)	17 (34%)	9 (18%)	
Hyperplasia	2 (4%)	- ()	(=,	1 (2%)	
Cyst	( )	2 (4%)	2 (4%)	1 (2%)	
Prostate	(50)	(50)	(50)	(50)	
Inflammation, Chronic	40 (80%)	32 (64%)	35 (70%)	25 (50%)	
Epithelium, Hyperplasia	4 (8%)	10 (20%)	2 (4%)	3 (6%)	
Testes	(50)	(50)	(50)	(50)	
Germinal Epithelium, Atrophy	12 (24%)	11 (22%)	24 (48%)	14 (28%)	
Interstitial Cell, Hyperplasia	6 (12%)	6 (12%)	8 (16%)	8 (16%)	

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DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
HEMATOPOIETIC SYSTEM					
Bone Marrow	(50)	(50)	(50)	(50)	
Myelofibrosis	2 (4%)	1 (2%)			
Hyperplasia	3 (6%)	7 (14%)	3 (6%)	1 (2%)	
Infiltration Cellular, Histiocyte			1 (2%)	1 (2%)	
Lymph Node	(18)	(14)	(16)	(13)	
Mediastinal, Ectasia	3 (17%)	1 (7%)	1 (6%)		
Mediastinal, Hemorrhage	2 (11%)	1 (7%)	4 (25%)	6 (46%)	
Mediastinal, Hyperplasia, Lymphoid	7 (39%)	5 (36%)	5 (31%)	7 (54%)	
Mediastinal, Pigmentation	2 (11%)	3 (21%)	5 (31%)	3 (23%)	
Pancreatic, Ectasia	, ,	,	1 (6%)	` ,	
Pancreatic, Hemorrhage	2 (11%)		2 (Ì3%́)	2 (15%)	
Pancreatic, Hyperplasia, Lymphoid	,	1 (7%)	2 (13%)	,	
Pancreatic, Pigmentation	1 (6%)	1 (7%)	,	3 (23%)	
Lymph Node, Mandibular	(0)	(1)	(4)	(1)	
Ectasia	( )	( )	2 (50%)	( )	
Hemorrhage			,	1 (100%)	
Lymph Node, Mesenteric	(50)	(50)	(50)	(50)	
Hemorrhage	10 (2Ó%)	3 (6%)	11 (22%)	6 (12%)	
Hyperplasia, Lymphoid	18 (36%)	15 (30%)	20 (40%)	15 (30%)	
Ectasia	3 (6%)	5 (10%)	3 (6%)	1 (2%)	
Pigmentation	15 (30%)	8 (16%)	16 (32%)	12 (24%)	
Spleen	(50)	(50)	(50)	(50)	
Hematopoietic Cell Proliferation	10 (2Ó%)	9 (18%)	11 (22%)	4 (8%)	
Pigmentation	9 (18%)	5 (10%)	6 (12%)	25 (50%)	
Fibrosis	2 (4%)	3 (6%)	2 (4%)	2 (4%)	
Necrosis	2 (4%)	1 (2%)	1 (2%)	1 (2%)	
Hemorrhage	= ( · · · · )	1 (2%)	(=75)	(=72)	
Lymphoid Follicle, Atrophy	1 (2%)	(-,-)	1 (2%)	2 (4%)	
Lymphoid Follicle, Hyperplasia	. (=,,,	1 (2%)	(=73)	1 (2%)	
Thymus	(49)	(46)	(46)	(49)	
Hemorrhage	1 (2%)	(13)	(10)	5 (10%)	
INTEGUMENTARY SYSTEM					
Mammary Gland	(49)	(48)	(47)	(48)	
Hyperplasia	31 (63%)	25 (52%)	29 (62%)	10 (21%)	
Skin	(49)	(50)	(50)	(50)	
Inflammation, Chronic	5 (10%)	1 (2%)	2 (4%)	2 (4%)	

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Test Type: CHRONIC

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a - Number of animals examined microscopically at site and number of animals with lesion

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Ulcer Cyst Epithelial Inclusion	4 (8%)	5 (10%) 4 (8%)	5 (10%) 2 (4%)	4 (8%)	
Epidermis, Hyperplasia Epidermis, Skin, Site Of Application, Hyperplasia	9 (18%) 1 (2%)	7 (14%) 10 (20%)	8 (16%) 29 (58%)	6 (12%) 19 (38%)	
Skin, Site Of Application, Erosion Skin, Site Of Application, Inflammation, Chronic		6 (12%)	1 (2%) 12 (24%)	11 (22%)	
MUSCULOSKELETAL SYSTEM					
Bone Cranium, Osteopetrosis	(50)	(50)	(50)	(50) 1 (2%)	
Femur, Osteopetrosis	1 (2%)			. (= /5)	
NERVOUS SYSTEM					
Brain Compression Hydrocephalus Hemorrhage Gliosis	(50) 16 (32%) 7 (14%) 1 (2%)	(50) 10 (20%) 1 (2%)	(50) 15 (30%) 5 (10%) 3 (6%) 1 (2%)	(50) 4 (8%) 2 (4%) 11 (22%) 2 (4%)	
Arteriole, Necrosis, Fibrinoid Neuron, Necrosis		1 (2%)		5 (10%) 16 (32%)	
RESPIRATORY SYSTEM					
Lung Infiltration Cellular, Histiocyte Hemorrhage Inflammation, Chronic Edema Metaplasia, Osseous Alveolar Epithelium, Hyperplasia Nose Foreign Body Inflammation, Chronic Respiratory Epithelium, Hyperplasia Respiratory Epithelium, Metaplasia,	(50) 21 (42%) 6 (12%) 9 (18%) 2 (4%)  10 (20%) (50) 13 (26%) 15 (30%) 11 (22%) 2 (4%)	(50) 19 (38%) 6 (12%) 13 (26%) 2 (4%) 2 (4%) 4 (8%) (50) 22 (44%) 22 (44%) 11 (22%)	(50) 21 (42%) 7 (14%) 16 (32%)  2 (4%) 6 (12%) (50) 12 (24%) 13 (26%) 8 (16%)	(50) 12 (24%) 17 (34%) 12 (24%) 2 (4%) 1 (2%) 6 (12%) (50) 12 (24%) 11 (22%) 9 (18%) 1 (2%)	

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a - Number of animals examined microscopically at site and number of animals with lesion

DIISOPROPYLCARBODIIMIDE CAS Number: 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS MALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Squamous					
SPECIAL SENSES SYSTEM					
Eye Cataract Cornea, Hyperplasia Cornea, Inflammation, Chronic Cornea, Ulcer Retina, Degeneration Harderian Gland Inflammation, Chronic Hyperplasia, Focal	(50) 4 (8%) (50)	(50) 1 (2%) 1 (2%) 1 (2%) (50) 1 (2%) 1 (2%)	(50) 2 (4%) 1 (2%) 5 (10%) 6 (12%) (50) 1 (2%)	(50) 1 (2%) 5 (10%) 23 (46%) 1 (2%) 3 (6%) (50) 1 (2%)	
URINARY SYSTEM					
Kidney Nephropathy Inflammation, Chronic Cyst Renal Tubule, Accumulation, Hyaline	(50) 43 (86%) 3 (6%)	(50) 46 (92%) 5 (10%) 1 (2%)	(50) 42 (84%) 9 (18%)	(50) 30 (60%) 1 (2%) 1 (2%)	
Droplet Renal Tubule, Dilatation Renal Tubule, Hyperplasia Renal Tubule, Necrosis Renal Tubule, Pigmentation Transitional Epithelium, Hyperplasia Urethra Angiectasis Urinary Bladder Hemorrhage Inflammation, Chronic Transitional Epithelium, Hyperplasia	1 (2%) 2 (4%) 2 (4%) (0) (50)	1 (2%) 4 (8%) (0) (50)	2 (4%)  1 (2%) (1) 1 (100%) (50) 1 (2%) 2 (4%) 1 (2%)	1 (2%) (0) (49) 3 (6%) 4 (8%)	

<sup>\*\*\*</sup> END OF MALE \*\*\*

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**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

**Date Report Reqsted:** 08/08/2005 **Time Report Reqsted:** 08:54:04 **First Dose M/F:** 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Disposition Summary					
•					
Animals Initially in Study	50	50	50	50	
Early Deaths Moribund Sacrifice	13	9	10	14	
Natural Death	7	9	8	10	
Survivors	,	3	0	10	
Terminal Sacrifice	30	32	32	25	
Other	33	02	02	1	
Animals Examined Microscopically	50	50	50	49	
. ,					
ALIMENTARY SYSTEM					
Intestine Large, Cecum	(50)	(50)	(50)	(49)	
Edema	1 (2%)	3 (6%)	1 (2%)	2 (4%)	
Inflammation, Chronic	(=/-)	1 (2%)	(= / - /	_ ( . , , ,	
Intestine Large, Rectum	(50)	(48)	(43)	(44)	
Hemorrhage	,	,	,	1 (2%)	
Intestine Small, Duodenum	(49)	(50)	(50)	( <del>4</del> 9)	
Epithelium, Hyperplasia	1 (2%)	,	` '	,	
Intestine Small, Jejunum	(47)	(50)	(50)	(46)	
Epithelium, Hyperplasia			1 (2%)		
Liver	(50)	(50)	(50)	(49)	
Basophilic Focus	42 (84%)	43 (86%)	45 (90%)	40 (82%)	
Infiltration Cellular, Mixed Cell	8 (16%)	11 (22%)	13 (26%)	8 (16%)	
Mixed Cell Focus	3 (6%)	5 (10%)	7 (14%)	1 (2%)	
Hematopoietic Cell Proliferation	1 (2%)		1 (2%)		
Necrosis, Focal	5 (10%)	1 (2%)	3 (6%)	4 (8%)	
Eosinophilic Focus	4 (8%)	3 (6%)	8 (16%)	5 (10%)	
Clear Cell Focus	10 (20%)	6 (12%)	4 (8%)	4 (8%)	
Hepatodiaphragmatic Nodule	11 (22%)	6 (12%)	12 (24%)	8 (16%)	
Regeneration	1 (2%)		- 4	2 (4%)	
Hemorrhage		1 (2%)	2 (4%)	1 (2%)	
Cyst			1 (2%)	. (22()	
Angiectasis	= (100()	0 (00()	1 (2%)	1 (2%)	
Bile Duct, Hyperplasia	5 (10%)	3 (6%)	2 (4%)	5 (10%)	
Centrilobular, Necrosis	1 (2%)	E (400()	0 (00()	2 (4%)	
Hepatocyte, Vacuolization Cytoplasmic	5 (10%)	5 (10%)	3 (6%)	4 (8%)	
Kupffer Cell, Pigmentation	1 (2%)	1 (2%)		1 (2%)	

a - Number of animals examined microscopically at site and number of animals with lesion

**TDMS No.** 93020 - 07

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DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS FEMALE					
	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Mesentery	(11)	(12)	(9)	(9)	
Fat, Necrosis	11 (100%)	11 (92%)	8 (89%)	9 (100%)	
Oral Mucosa	(1)	(0)	(2)	(0)	
Cyst			1 (50%)		
Pancreas	(50)	(50)	(50)	(49)	
Atrophy	15 (30%)	16 (32%)	18 (36%)	19 (39%)	
Cyst	4 (8%)	6 (12%)	5 (10%)		
Necrosis				1 (2%)	
Acinus, Cytoplasmic Alteration		1 (2%)	1 (2%)		
Acinus, Hyperplasia, Focal		1 (2%)	1 (2%)		
Salivary Glands	(50)	(50)	(50)	(48)	
Atrophy	3 (6%)	1 (2%)	1 (2%)	1 (2%)	
Stomach, Forestomach	(50)	(50)	(50)	(49)	
Ulcer	3 (6%)		1 (2%)	4 (8%)	
Edema	2 (4%)		1 (2%)	2 (4%)	
Epithelium, Hyperplasia	4 (8%)	(50)	2 (4%)	2 (4%)	
Stomach, Glandular	(50)	(50)	(50)	(49)	
Erosion Ulcer	1 (2%)	1 (2%) 1 (2%)	2 (4%) 1 (2%)	4 (8%) 1 (2%)	
Edema		1 (2%)	1 (2%)	1 (2%)	
Glands, Hyperplasia	1 (2%)		1 (2%)	1 (2/8)	
Giarius, rryperpiasia	1 (270)		1 (270)		
CARDIOVASCULAR SYSTEM					
Heart	(50)	(50)	(50)	(49)	
Cardiomyopathy	30 (60%)	39 (78%)	35 (70%)	31 (63%)	
Thrombosis	1 (2%)	1 (2%)	1 (2%)	1 (2%)	
Inflammation, Chronic	` ,	1 (2%)	, ,	1 (2%)	
ENDOCRINE SYSTEM					
Adrenal Cortex	(50)	(50)	(50)	(49)	
Degeneration, Fatty	20 (40%)	15 (30%)	16 (32%)	17 (35%)	
Hyperplasia, Focal	3 (6%)	,	4 (8%)	5 (10%)	
Hypertrophy, Focal	10 (20%)	10 (20%)	9 (18%)	8 (16%)	
Accessory Adrenal Cortical Nodule	9 (18%)	6 (12%)	9 (18%)	8 (16%)	
Adrenal Medulla	(49)	(50)	(50)	(49)	
Hyperplasia	5 (10%)	2 (4%)	4 (8%)	2 (4%)	
Islets, Pancreatic	(50)	(50)	(50)	(49)	
Hyperplasia	1 (2%)		2 (4%)		

a - Number of animals examined microscopically at site and number of animals with lesion

**TDMS No.** 93020 - 07

Test Type: CHRONIC

Route: SKIN APPLICATION

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

**Date Report Reqsted:** 08/08/2005 **Time Report Reqsted:** 08:54:04 **First Dose M/F:** 04/24/00 / 04/24/00

Lab: SRI

FIGURED 244 DATO FEMALE					
FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Metaplasia, Hepatocyte		1 (2%)			
Pituitary Gland	(50)	(50)	(50)	(49)	
Pars Distalis, Angiectasis	1 (2%)	6 (12%)	4 (8%)	4 (8%)	
Pars Distalis, Cyst	16 (32%)	6 (12%)	15 (30%)	14 (29%)	
Pars Distalis, Hyperplasia, Focal	7 (14%)	7 (14%)	10 (20%)	11 (22%)	
Pars Intermedia, Angiectasis		1 (2%)	2 (4%)	2 (4%)	
Pars Intermedia, Cyst	1 (2%)	1 (2%)	2 (4%)		
Thyroid Gland	(50)	(50)	(50)	(49)	
Ultimobranchial Cyst				2 (4%)	
C-cell, Hyperplasia	17 (34%)	14 (28%)	10 (20%)	12 (24%)	
Follicle, Cyst	2 (4%)	2 (4%)	3 (6%)	1 (2%)	
Follicular Cell, Hyperplasia	1 (2%)		1 (2%)	1 (2%)	
ENERAL BODY SYSTEM  None					
ENITAL OVOTEM					
ENITAL SYSTEM					
Clitoral Gland	(50)	(49)	(50)	(49)	
Inflammation, Chronic	13 (26%)	2 (4%)	10 (20%)	3 (6%)	
Cyst	1 (2%)	3 (6%)	1 (2%)	3 (6%)	
Hyperplasia		2 (4%)	2 (4%)		
Ovary	(50)	(50)	(50)	(49)	
Cyst	11 (22%)	8 (16%)	9 (18%)	6 (12%)	
Angiectasis	1 (2%)				
Corpus Luteum, Hyperplasia	1 (2%)				
Uterus	(50)	(50)	(50)	(49)	
Endometrium, Hyperplasia, Cystic	4 (8%)	10 (20%)	5 (10%)	9 (18%)	
Vagina	(6)	(6)	(5)	(11)	
Inflammation, Chronic	1 (17%)				
Cyst	1 (17%)	1 (17%)			
EMATOPOIETIC SYSTEM					
Bone Marrow	(50)	(50)	(50)	(49)	
Hyperplasia	6 (12 <sup>′</sup> %)	8 (16 <sup>6</sup> %)	3 (6%)	6 (12 <sup>′</sup> %)	
	` '		2 (4%)		
Myelofibrosis		1 (2%)	Z (470)	2 (4%)	

**TDMS No.** 93020 - 07

Test Type: CHRONIC

Route: SKIN APPLICATION

a - Number of animals examined microscopically at site and number of animals with lesion

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

Lymph Node Deep Cervical, Hemorrhage Deep Cervical, Hyperplasia, Lymphoid Deep Cervical, Pigmentation	(13) 4 (31%)	(10) 1 (10%) 1 (10%) 1 (10%)	(14)	(8)	
Deep Cervical, Hemorrhage Deep Cervical, Hyperplasia, Lymphoid Deep Cervical, Pigmentation		1 (10%) 1 (10%)	(14)	(8)	
Deep Cervical, Hyperplasia, Lymphoid Deep Cervical, Pigmentation	4 (31%)	1 (10%)			
Deep Cervical, Pigmentation	4 (31%)				
	4 (31%)	1 (10%)			
	4 (31%)				
Mediastinal, Ectasia	4 (31%)		1 (7%)		
Mediastinal, Hemorrhage		4 (40%)	4 (29%)	3 (38%)	
Mediastinal, Hyperplasia, Lymphoid	3 (23%)	5 (50%)	7 (50%)		
Mediastinal, Pigmentation	6 (46%)	6 (60%)	9 (64%)	2 (25%)	
Pancreatic, Hemorrhage	1 (8%)	3 (30%)	1 (7%)	1 (13%)	
Pancreatic, Hyperplasia, Lymphoid		1 (10%)			
Pancreatic, Pigmentation	1 (8%)	2 (20%)	1 (7%)	1 (13%)	
Lymph Node, Mandibular	(3)	(7)	(1)	(2)	
Ectasia	1 (33%)	4 (57%)	. ,	1 (50%)	
Hyperplasia, Lymphoid	1 (33%)	` ,		, ,	
Pigmentation	1 (33%)	1 (14%)			
Lymph Node, Mesenteric	(50)	(50)	(50)	(48)	
Pigmentation	25 (50%)	24 (48%)	27 (54%)	17 (35%)	
Hemorrhage	11 (22%)	11 (22%)	6 (Ì2%)	5 (10%)	
Hyperplasia, Lymphoid	16 (32%)	20 (40%)	12 (24%)	11 (23%)	
Ectasia	,	1 (2%)	,	1 (2%)	
Necrosis		,		1 (2%)	
Spleen	(50)	(50)	(50)	(49)	
Pigmentation	10 (20%)	16 (32%)	13 (26%)	16 (33%)	
Hematopoietic Cell Proliferation	21 (42%)	29 (58%)	29 (58%)	20 (41%)	
Necrosis	1 (2%)	1 (2%)	2 (4%)	,	
Fibrosis	,	1 (2%)	,	2 (4%)	
Hemorrhage		,		2 (4%)	
Hyperplasia, Reticulum Cell				1 (2%)	
Lymphoid Follicle, Atrophy		2 (4%)		1 (2%)	
Lymphoid Follicle, Hyperplasia	1 (2%)	, ,	3 (6%)	1 (2%)	
Thymus	(50)	(48)	(49)	(46)	
Hyperplasia, Lymphoid	1 (2%)	2 (4%)	1 (2%)	1 (2%)	
Hemorrhage	2 (4%)	2 (4%)	1 (2%)	1 (2%)	
INTEGUMENTARY SYSTEM					
Mammary Gland	(50)	(50)	(50)	(48)	
Hyperplasia	45 (90%)	46 (92%)	45 (90%)	41 (85%)	
Skin	(50)	(50)	(50)	(49)	
Inflammation, Chronic	2 (4%)	1 (2%)	(50)	(73)	

**TDMS No.** 93020 - 07

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a - Number of animals examined microscopically at site and number of animals with lesion

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

Date Report Reqsted: 08/08/2005 Time Report Reqsted: 08:54:04 First Dose M/F: 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
Cyst Epithelial Inclusion		1 (2%)	4 (00()		
Ulcer Epidermis, Skin, Site Of Application,	1 (2%)	5 (10%)	1 (2%) 16 (32%)	21 (43%)	
Hyperplasia	0 (40/)	2 (40/)	0 (40()	4 (20/)	
Epidermis, Hyperplasia Skin, Site Of Application, Inflammation, Chronic	2 (4%)	2 (4%)	2 (4%) 3 (6%)	1 (2%) 10 (20%)	
MUSCULOSKELETAL SYSTEM					
None					
NERVOUS SYSTEM					
Brain	(50)	(50)	(50)	(49)	
Compression	14 (28%)	13 (26%)	14 (28%)	13 (27%)	
Hydrocephalus Necrosis	2 (4%) 2 (4%)	8 (16%) 1 (2%)	1 (2%) 2 (4%)	2 (4%)	
Gliosis	1 (2%)	1 (2%)	2 (4%)		
Hemorrhage	1 (2%)	8 (16%)			
Angiectasis	1 (2%)		1 (2%)		
RESPIRATORY SYSTEM					
Lung	(50)	(50)	(50)	(49)	
Inflammation, Chronic	10 (20%)	22 (44%)	19 (38%)	10 (20%) 27 (55%)	
Infiltration Cellular, Histiocyte Hemorrhage	22 (44%) 8 (16%)	26 (52%) 14 (28%)	30 (60%) 9 (18%)	27 (55%) 13 (27%)	
Metaplasia, Squamous	1 (2%)	11 (2070)	1 (2%)	10 (21 70)	
Edema	4 (8%)	4 (8%)	3 (6%)	2 (4%)	
Metaplasia, Osseous			2 (4%)	1 (2%)	
Emphysema Pigmentation			1 (2%)	1 (2%)	
Alveolar Epithelium, Hyperplasia	3 (6%)	4 (8%)	10 (20%)	1 (2%)	
Nose	(50)	(50)	(50)	(49)	
Foreign Body	5 (10%)		2 (4%)	3 (6%)	
Inflammation, Chronic Respiratory Epithelium, Hyperplasia	6 (12%) 4 (8%)	1 (2%) 1 (2%)	2 (4%) 2 (4%)	3 (6%) 1 (2%)	
Respiratory Epitrielium, rryperplasia	4 (070)	I (Z70)	Z (470)	1 (270)	

**TDMS No.** 93020 - 07

Test Type: CHRONIC

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a - Number of animals examined microscopically at site and number of animals with lesion

DIISOPROPYLCARBODIIMIDE

**CAS Number:** 693-13-0

Pathologist: HEATH, J. - DURBIN, L. - ALLISON, M.

**Date Report Reqsted:** 08/08/2005 **Time Report Reqsted:** 08:54:04 **First Dose M/F:** 04/24/00 / 04/24/00

Lab: SRI

FISCHER 344 RATS FEMALE	0 MG/KG	10 MG/KG	20 MG/KG	40 MG/KG	
SPECIAL SENSES SYSTEM					
	(50)	(50)	(50)	(49)	
Eye Cataract	2 (4%)	5 (10%)	(50) 3 (6%)	3 (6%)	
Cornea, Hyperplasia	2 (170)	0 (1070)	0 (070)	3 (6%)	
Cornea, Inflammation, Chronic	1 (2%)	1 (2%)		3 (6%)	
Retina, Degeneration	4 (8%)	7 (14%)	5 (10%)	4 (8%)	
Retina, Dysplasia	(50)	(50)	1 (2%)	(40)	
Harderian Gland Hyperplasia, Focal	(50)	(50)	(50)	(49)	
Inflammation, Chronic	1 (2%)	1 (2%)			
URINARY SYSTEM					
Kidney	(50)	(50)	(50)	(49)	
Nephropathy	32 (64%)	32 (64%)	28 (56%)	21 (43%)	
Inflammation, Suppurative	1 (2%)				
Cyst	1 (2%)	0 (40()	4 (00()		
Inflammation, Chronic Infarct	2 (4%) 1 (2%)	2 (4%)	1 (2%) 1 (2%)		
Hemorrhage	1 (2/0)		1 (2/0)	1 (2%)	
Papilla, Necrosis				1 (2%)	
Renal Tubule, Accumulation, Hyaline	2 (4%)	1 (2%)		2 (4%)	
Droplet	, ,	, ,			
Renal Tubule, Dilatation	1 (2%)	- (101)	1 (2%)	1 (2%)	
Renal Tubule, Necrosis	1 (2%)	2 (4%)	4 (20()	2 (4%)	
Transitional Epithelium, Hyperplasia Urinary Bladder	(50)	(50)	1 (2%) (50)	(49)	
Hemorrhage	(30)	(50)	1 (2%)	(43)	

<sup>\*\*\*</sup> END OF REPORT \*\*\*

**TDMS No.** 93020 - 07

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